

September 18, 1961

Dr. George Klein  
Institute for Tumor Biology  
Karolinska Institutet  
Stockholm 60, Sweden

Dear George:

Just a brief remark about the mechanism of action of ultraviolet light which we had discussed briefly in connection with Halliday's paper in Genetical Research. I think I would now agree that there was room for the hypothesis that UV augments the pairing of homologous chromosomes in mitotic crossing-over as well, perhaps, as initiating potential breaks that also lead to crossing-over. But this does not have to be a regular normal process in the mitotic mechanism. Rather, I would think that the effect of UV light is to upset the usual differentiation of the chromosomes so that they are able to form abnormal associations that would otherwise be hindered in the prophase nucleus. One way of saying this which is, of course, rather vague from a chemical standpoint, is that the differentiating chromosomes become rather sticky. There is, perhaps, some support for this in the effects of UV light on bacteria, e.g., as I discussed in the 1951 Cold Spring Harbor Symposium - see page 428, middle paragraph on the right hand side, and figure 9 B on page 427. I have not been thinking about this problem lately, and am appreciative that you pointed out the necessary elements to make a connection. Whether there would be quite a similar disorganization of the whole mitotic process in the nuclei of mammalian cells is, of course, another question. But the concept does again lend weight to the desirability of experiments on the effect of agents like aminopterin on somatic crossing-over.

To Eva - Unfortunately, experiment 1473 did not work out so very well (see the notes that I sent you on September 8). Haruko picked a great many colonies, but on this occasion, only the rather small fraction of the small colonies were transformant clones, and most of the transformants were represented by medium sized and even some larger colonies. I suppose we really have to go back to the original question of the mechanism of the delay in the growth of these competent cells as it is quite possible that we used cells in this experiment that were rather far along in competence and therefore did not have very much more delay to mark them as producing smaller colonies. At least this is what I have to think was wrong with this experiment and the cause of the discrepancy between it and the previous run which showed the transformants to be all in small colonies.

Haruko is doing very well indeed in executing these experiments and will probably need only some brief supervision and discussion every day to follow them through. So I have been thinking that I might spend most of my own time during the next months on experiments on the replication of DNA or rather transforming activity. We have had some unsuccessful attempts at doing this with the purified

preparations of DNA polymerase that Kornberg prepared. But obviously the intact cell accomplishes this replication and we might try some experiments on less purified, more complete systems like protoplasts and particulate preparations. I hope you will not be disinterested to be kept informed on the continuity of our program, and needless to say, any suggestions you may have to make would be most welcome.

Our thanks to both of you for your very kind letter, and also especially to Peter - we really hope that he will be able to sustain the remarkable performance he made in starting English.

Unfortunately, the season is beginning again when I will have to spend a little less time in the laboratory and more on some trips, but at least this will give the advantage of seeing Caspersson again as Elliott and I hope to do in about two weeks.

I saw Rosarai by chance the other day, and found that her car will unfortunately still not be ready for another couple of weeks, since they have to obtain some difficult parts. This is too bad, but of course, there can be no help for it and it should be of no concern to you, but please let me know if there are loose ends of a business or similar character that we might be of any help in. Knowing your capacity for organization, George, I would not expect this, but if anything does come up, please let us hear about it.

Yours sincerely,

Joshua Lederberg